AP
IDW

FULBRIGHT & JAWORSKI L.L.P.
A REGISTERED LIMITED LIABILITY PARTNERSHIP
600 CONGRESS AVENUE, SUITE 2400
AUSTIN, TEXAS 78701-3271
WWW.FULBRIGHT.COM

DAVID L. PARKER
PARTNER
DPARKER@FULBRIGHT.COM

DIRECT DIAL: (512) 536-3055
TELEPHONE: (512) 474-5201
FACSIMILE: (512) 536-4598

December 20, 2004

CERTIFICATE OF MAILING
37 C.F.R. 1.8

I hereby certify that this correspondence is being deposited with the U.S. Postal Service with sufficient postage as First Class Mail in an envelope addressed to: Commissioner for Patents, P. O. Box 1450, Alexandria, VA 22313-1450, on the date below:

December 20, 2004 — Date
David L. Parker

MS Appeal Briefs
Commissioner for Patents
P. O. Box 1450
Alexandria, VA 22313-1450

Re: *SN 09/415,890 entitled "Pharmacologically Acceptable Solvent Vehicles" by Andersson*
Our ref: UTXC:528--1 Client ref: MDA96-033 CON1

Commissioner:

Enclosed please find the following for filing in the above-referenced patent application:

1. Supplemental Appeal Brief, with Appendices A and B (consisting of Exhibits 1-3) (original and three copies); and

2. A return postcard to acknowledge receipt of these materials. Please date stamp this postcard and return it by mail.

Should any fees under 37 C.F.R. §§ 1.16 to 1.21 be required for any reason relating to the enclosed materials, the Commissioner is authorized to deduct said fees from Fulbright & Jaworski L.L.P. Account No.: 50-1212/UTXC:528--1

Very truly yours,

David L. Parker
Reg. No. 32,165

DLP/ld
Enclosures

25484703.1 / 10016657

CERTIFICATE OF MAILING
37 C.F.R. 1.8

I hereby certify that this correspondence is being deposited with the U.S. Postal Service with sufficient postage as First Class Mail in an envelope addressed to: Commissioner for Patents, P. O. Box 1450, Alexandria, VA 22313-1450, on the date below:

December 20, 2004
Date

David L. Parker

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:
Borje S. Andersson

Serial No.: 09/415,890

Filed: October 8, 1999

For: PHARMACOLOGICALLY ACCEPTABLE SOLVENT VEHICLES

Group Art Unit: 1616

Examiner: Neil Levy

Atty. Dkt. No.:UTXC:528--1/DLP

SUPPLEMENTAL APPEAL BRIEF

MS Appeal Briefs
Commissioner for Patents
P. O. Box 1450
Alexandria, VA 22313-1450

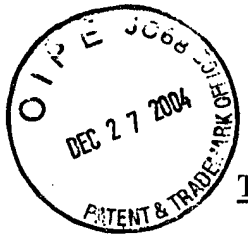


TABLE OF CONTENTS

Sir:

Appellants hereby submit an original and three copies of this Supplemental Appeal Brief to the Board of Patent Appeals and Interferences pursuant to 37 C.F.R. §1.193(b)(2)(ii) in response to the Office Action dated September 20, 2004. It is therefore believed that the filing of the present Supplemental Appeal Brief is timely and, since the appeal brief filing fee has previously been paid, it is believed that no fees are due. However, if any fees are due for any reason relating to the enclosed materials, the Commissioner is authorized to deduct said fees from Fulbright & Jaworski L.L.P. Account No.: 50-1212/UTXC:528--1.

Please date stamp and return the attached postcard as evidence of receipt.

I. REAL PARTY IN INTEREST

The real party in interest is the assignee, Board of Regents, The University of Texas System, Austin, Texas and its licensee, Ceptyr, Inc.

II. RELATED APPEALS AND INTERFERENCES

There are no interferences or appeals for related cases.

III. STATUS OF THE CLAIMS

Claims 94-99 and 106-150 are currently pending, with claims 94-96, 106-115, 123-132, 138-140 and 144-149 currently withdrawn as being directed to a non-elected invention and species with no currently allowable generic or linking claim. Claims 97, 99, 116, 117, 119, 121, 122, 133, 141 and 150 are currently subject to rejection. No rejection has been entered with respect to claims 118, 120, 134-137, 142 and 143. Appellants are appealing the rejection of claims 97, 99, 116, 117, 119, 121, 122, 133, 141 and 150. A copy of the claims on appeal, as well as the other pending claims, is attached as Appendix A.

IV. STATUS OF AMENDMENTS

All previously sought amendments have been entered.

V. SUMMARY OF THE CLAIMED SUBJECT MATTER

The present invention is directed to a method for making a solvent vehicle for use in solubilizing drugs, particularly relatively insoluble drugs, through the application of a process such as embodied in claim 97, which reads as follows:

> 97. A method for preparing a pharmaceutically acceptable solvent vehicle, the method comprising:
>
> (a) obtaining a pharmaceutically acceptable dipolar aprotic solvent and/or acid;
>
> *(see page 4, line 20, for example; the use of acids such as acetic acid instead of dipolar aprotic solvents is described in the paragraph bridging pages 13-14)*
>
> (b) mixing the dipolar aprotic solvent and/or acid in a pharmaceutically acceptable aqueous secondary solvent;
>
> *(see page 4, lines 22-30)*
>
> (c) removing more than 50% of the dipolar aprotic solvent and/or acid and aqueous secondary solvent; and
>
> *(see page 5, lines 12-16)*
>
> (d) reconstituting the solvent vehicle by the addition of a pharmaceutically acceptable aqueous solvent.
>
> *(see page 5, lines 16-21)*

The dependent claims further specify particular types of solvents or acid as well as the inclusion of lipids, such as in the form of lipid emulsions and in particular soybean emulsion. *(see page 4, lines 24-28)*

VI. GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

The issues addressed in this appeal include:

a) Whether the subject matter of claims 97 and 116 is anticipated by Stehle *et al.* GB 145732 (Exhibit 1);

b) Whether the subject matter of claims 97, 99, 116, 117 and 119 are anticipated by Janoff *et al.* 6,406,713 (Exhibit 2);

c) Whether the subject matter of claims 97, 99, 116, 119 and 133 are obvious over Janoff in view of Szoka, U.S. 5,277,914 (Exhibit 3);

d) Whether the subject matter of claims 97, 99, 116, 117, 121, 122, 141 and 150 is obvious over claims 25, 27, 28, 30-32 and 34 of copending USSN 10/294,491;

e) Whether the subject matter of claims 97, 99, 116, 119, 121, 122 and 133 is obvious over claims 45-63 of copending USSN 10/439,252.

VII. ARGUMENT

A. Rejection of Claims 97 and 116 as Anticipated by Stehle *et al.*, GB 145732.

The Action first rejects claims 97 and 116 as anticipated by Stehle *et al.* ("Stehle"), GB 145732 (Exhibit 1). The Action takes the position that example 1 of Stehle discloses mixing DMSO or DMA with a co-solvent, water and that then the solvent is removed by filtration. We respectfully traverse.

In response, it is clear that no *prima facie* rejection has been made out by the Action. The "filtration" referred to in example 1 of Stehle appears to refer simply to the use of a micro-porous, solvent resistant filter for the purpose of sterilizing the drug/DMA solution. The Action has failed to explain how the reference teaches each step of claims 97 and 116 and thus has failed to make out a *prima facie* rejection.

B. Rejection of Claims 97, 99, 116, 117 and 119 as Anticipated by Janoff *et al.*, US 6,406,713

The Action next rejects claims 97, 99, 116, 117 and 119 as anticipated by Janoff *et al.*, US 6,406,713 ("Janoff"). The Action takes the position that the teachings at col. 4, lines 46-64, anticipate the subject matter of the rejected claims. We respectfully traverse.

We again take the position that the Action fails to set forth a *prima facie* anticipation rejection of the subject claims.

Turning first to claims 97, 99 and 116, Appellants point out that Janoff appears to teach dissolving the drug in DMSO or methanol, so there is no aqueous solvent here (see col. 4, lines 49-50). It also teaches solubilizing lipids in "a solvent such as methylene chloride," (col. 4, lines 50-52) so, again, no aqueous solvent here. It is not until the solvents are "evaporated under reduced pressure" that an aqueous solution is added for the first time. (col. 4, lines 54-56). Janoff does refer to an alternative where the aqueous solvent is added *prior* to evaporation of the solvent (col. 4, lines 56-58), however, here it is stated that only the solvent is removed ("...evaporation of the solvent") and there is no teaching to undertake the addition of a pharmaceutically acceptable aqueous solvent. Thus, the Action has failed to set forth a *prima facie* anticipation rejection of claim 97.

Turning next to claim 117, the Action also fails to show where Janoff teaches an "aqueous lipid emulsion." The Action refers us to col. 11, lines 14-19, however, while this excerpt makes reference to homogenization, it says nothing about the use of an aqueous lipid emulsion. Thus, no *prima facie* anticipation rejection has been set forth for claim 117 for this reason and the reasons set forth above.

Turning next to claim 119, the Action also fails to show where Janoff teaches an "aqueous soy bean lipid emulsion." The Action refers us to the last paragraph of col. 8, however, this paragraph makes reference only to phospholipids, including "soybean PC" ("phosphatidylcholine") and says nothing about an aqueous soy bean lipid emulsion. Thus, no *prima facie* anticipation rejection has been set forth for this reason and the reasons set forth above.

C. Rejection of Claims 97, 99, 116, 117, 119, 133 as Obvious over Janoff in view of Szoka

1. Summary of Rejection

The Action next rejects claims 97, 99, 116, 117, 119 and 133 as obvious over Janoff in view of Szoka, US 5,277,914 (Exhibit 3). The Action relies upon Janoff as discussed above and relies upon Szoka merely for it teaching of solvents other than DMSO, such as DMF. We respectfully traverse.

2. Appellant's Remarks

a) Substantial evidence required to uphold the examiner's position

Findings of fact and conclusions of law by the U.S. Patent and Trademark Office must be made in accordance with the Administrative Procedure Act, 5 U.S.C. § 706(A), (E), 1994. *Dickinson v. Zurko*, 527 U.S. 150, 158 (1999). Moreover, the Federal Circuit has held that findings of fact by the Board of Patent Appeals and Interferences must be supported by "substantial evidence" within the record. *In re Gartside*, 203 F.3d 1305, 1315 (Fed. Cir. 2000). In *In re Gartside*, the Federal Circuit stated that "the 'substantial evidence' standard asks whether a reasonable fact finder could have arrived at the agency's decision." *Id.* at 1312.

Accordingly, it necessarily follows that an Examiner's position on Appeal must be supported by "substantial evidence" within the record in order to be upheld by the Board of Patent Appeals and Interferences.

b) The standard for obviousness

In order to establish a *prima facie* case of obviousness, three basic criteria must be met: (1) there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings; (2) there must be a reasonable expectation of success; and (3) the

prior art reference (or references when combined) must teach or suggest all the claim limitations. *Manual of Patent Examining Procedure* § 2142. Moreover, the teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on Applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 U.S.P.Q. 2d 1438 (Fed Cir. 1991). When "the motivation to combine the teachings of the references is not immediately apparent, it is the duty of the examiner to explain why the combination of the teachings is proper." MPEP § 2142.

c) No Proper Prima Facie Rejection Made

Appellants incorporate by reference the arguments set forth above in the anticipation sections, and further note that the Action does not purport to cite Szoka for the purpose of addressing any of the shortcomings in the anticipation rejections, and indeed, Szoka does not supply the missing teachings. Thus, even if Szoka is properly combinable with Janoff, no *prima facie* obviousness rejection has been set forth.

For the foregoing reasons, the Examiner is requested to reconsider and withdraw the rejection, and permit applicant the right to reintroduce the withdrawn claims.

D. Provisional Rejection of Claims 97, 99, 116, 117, 121, 122, 141 and 150 as obvious over claims 25, 27, 28, 30-32 and 34 of copending USSN 10/294,491

The Board is advised that the claims of USSN 10/294,491 have been allowed and the assignee is preparing to pay the issue fee. Appellants are amenable to submitting a terminal disclaimer over any patent that might issue on the '491 application, but not that at the present time the rejection is still provisional.

E. Provisional Rejection of Claims 97, 99, 116, 119, 121, 122 and 133 as obvious over claims 45-63 of copending USSN 10/439,252

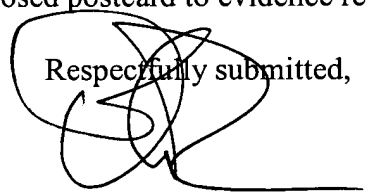
The Board is advised that since USSN 10/439,252 is still pending and has not issued, the present rejection is still provisional. It is unknown whether the '252 application will ever issue and, if so, what claims will issue.

VIII. CONCLUSION

Appellant has provided arguments that overcome the pending rejections. Appellant respectfully submits that the Final Official Action's conclusions that the claims should be rejected are unwarranted. It is therefore requested that the Board overturn the Final Action's rejections.

Please date stamp and return the enclosed postcard to evidence receipt of this document.

Respectfully submitted,



David L. Parker
Reg. No. 32,165
Attorney for Appellant

FULBRIGHT & JAWORSKI L.L.P
600 Congress Avenue, Suite 2400
Austin, Texas 78701
512.536.3055 (voice)
512.536.4598 (fax)

Date: December 20, 2004

APPENDIX A

CLAIMS APPENDIX

APPENDIX A

CLAIMS

1.-93. (Cancelled)

94. (Withdrawn) The method of claim 93, where the acid is acetic acid.

95. (Withdrawn) The method of claim 93, where the dipolar aprotic solvent and/or acid is virtually eliminated from the solvent vehicle.

96. (Withdrawn) The method of claim 93, where removing the dipolar aprotic solvent and/or acid is by lyophilization.

97. (Previously Presented) A method for preparing a pharmaceutically acceptable solvent vehicle, the method comprising:

(a) obtaining a pharmaceuctically acceptable dipolar aprotic solvent and/or acid;

(b) mixing the dipolar aprotic solvent and/or acid in a pharmaceutically acceptable aqueous secondary solvent;

(c) removing more than 50% of the dipolar aprotic solvent and/or acid and aqueous secondary solvent; and

(d) reconstituting the solvent vehicle by the addition of a pharmaceutically acceptable aqueous solvent.

98. (Cancelled)

99. (Previously Presented) The method of claim 97, further comprising the step of dissolving pimaricin in said dipolar aprotic solvent and/or acid prior to mixing in a pharmaceutically acceptable aqueous secondary solvent.

100.-105. (Cancelled)

106. (Withdrawn) The method of claim 93, wherein the dipolar aprotic solvent or acid is eliminated.

107. (Withdrawn) The method of claim 93, wherein the removing dipolar aprotic solvent or acid removes 95% of the dipolar aprotic solvent or acid.

108. (Withdrawn) The method of claim 107, wherein the removing dipolar aprotic solvent or acid removes 99% of the dipolar aprotic solvent or acid.

109. (Withdrawn) The method of claim 93, wherein said aprotic solvent comprises N,N-dimethylacetamide, castor oil, dimethylsulfoxide, 1,2,-propylene-diol, glycerol or polyethylene glycol-400.

110. (Withdrawn) The method of claim 109, wherein said aprotic solvent comprises N,N-dimethylacetamide.

111. (Withdrawn) The method of claim 109, wherein said aprotic solvent comprises castor oil.

112. (Withdrawn) The method of claim 109, wherein said aprotic solvent comprises dimethylsulfoxide.

113. (Withdrawn) The method of claim 109, wherein said aprotic solvent comprises 1,2,-propylene-diol.

114. (Withdrawn) The method of claim 109, wherein said aprotic solvent comprises glycerol.

115. (Withdrawn) The method of claim 109, wherein said aprotic solvent comprises polyethylene glycol-400.

116. (Previously Presented) The method of claim 97, wherein said secondary solvent comprises aqueous lipid emulsion, water, saline solution, dextrose solution, glacial acetic acid, or lipid solution.

117. (Previously Presented) The method of claim 116, wherein said secondary solvent comprises an aqueous lipid emulsion.

118. (Previously Presented) The method of claim 117, wherein said aqueous lipid emulsion comprises emulsified fat particles of about 0.4 micron in diameter.

119. (Previously Presented) The method of claim 117, wherein said aqueous lipid emulsion comprises an aqueous soy bean lipid emulsion.

120. (Previously Presented) The method of claim 119, wherein said aqueous soy bean lipid emulsion comprises soy bean oil, lecithin, glycerin and water.

121. (Previously Presented) The method of claim 117, wherein said aqueous lipid emulsion comprises a lipid component that includes at least one vegetable oil and at least one fatty acid.

122. (Previously Presented) The method of claim 121, wherein said lipid component comprises at least about 5% by weight soybean oil and at least about 50% by weight fatty acids.

123. (Withdrawn) The method of claim 116, wherein said secondary solvent comprises water.

124. (Withdrawn) The method of claim 116, wherein said secondary solvent comprises saline solution.

125. (Withdrawn) The method of claim 116, wherein said secondary solvent comprises dextrose solution.

126. (Withdrawn) The method of claim 125, wherein said dextrose solution comprises 5% to 70% dextrose in water.

127. (Withdrawn) The method of claim 126, wherein said dextrose solution comprises 5% or 10% dextrose solution.

128. (Withdrawn) The method of claim 116, wherein said secondary solvent comprises glacial acetic acid.

129. (Withdrawn) The method of claim 93, wherein said secondary solvent comprises a lipid solution.

130. (Withdrawn) The method of claim 93, wherein said secondary solvent comprises a parenteral infusion fluid.

131. (Withdrawn) The method of claim 93, wherein said solvent vehicle comprises anhydrous N,N-dimethylacetamide and polyethylene glycol-400.

132. (Withdrawn) The method of claim 93, wherein said solvent vehicle comprises glacial acetic acid and polyethylene glycol-400.

133. (Previously Presented) The method of claim 97, wherein said solvent vehicle comprises anhydrous N,N-dimethylacetamide and aqueous lipid.

134. (Previously Presented) The method of claim 133, wherein said aqueous lipid is an aqueous soy bean lipid emulsion comprising soy bean oil, lecithin, glycerin and water.

135. (Previously Presented) The method of claim 134, wherein said solvent vehicle comprises anhydrous N,N,-dimethylacetamide and an aqueous soy bean lipid emulsion comprising soy bean oil, lecithin, glycerin and water in a 1:10 volume ratio.

136. (Previously Presented) The method of claim 134, wherein said solvent vehicle comprises anhydrous N,N,-dimethylacetamide diluted with 9 volumes 20% of an aqueous soy bean lipid emulsion comprising soy bean oil, lecithin, glycerin and water.

137. (Previously Presented) The method of claim 134, wherein said solvent vehicle further comprises normal saline or 5% dextrose solution.

138. (Withdrawn) The method of claim 93, wherein said solvent vehicle comprises anhydrous N,N-dimethylacetamide, polyethylene glycol-400 and 1,2-propylene diol.

139. (Withdrawn) The method of claim 93, wherein said solvent vehicle comprises anhydrous N,N-dimethylacetamide, polyethylene glycol-400, 1,2-propylene diol and dimethylsulfoxide.

140. (Withdrawn) The solvent vehicle of claim 139, wherein said solvent vehicle comprises anhydrous N,N,-dimethylacetamide, polyethylene glycol-400, 1,2-propylene diol and dimethylsulfoxide in equal volume ratios.

141. (Previously Presented) The method of claim 97, wherein said vehicle comprises glacial acetic acid, and wherein said vehicle further comprises anhydrous N,N,-dimethylacetamide, dimethylsulfoxide or an aqueous soy bean lipid emulsion comprising soy bean oil, lecithin, glycerin and water.

142. (Previously Presented) The method of claim 150, wherein said solvent vehicle comprises glacial acetic acid, dimethylsulfoxide and an aqueous soy bean lipid emulsion comprising soy bean oil, lecithin, glycerin and water.

143. (Previously Presented) The method of claim 142, wherein said solvent vehicle comprises glacial acetic acid, dimethylsulfoxide, and an aqueous soy bean lipid emulsion comprising soy bean oil, lecithin, glycerin and water in a 2:6:3 volume ratio.

144. (Withdrawn) The method of claim 98, wherein said pharmaceutically acceptable aqueous solution comprises water.

145. (Withdrawn) The method of claim 98, wherein said pharmaceutically acceptable aqueous solution comprises saline solution.

146. (Withdrawn) The method of claim 98, wherein said pharmaceutically acceptable aqueous solution comprises dextrose solution.

147. (Withdrawn) The method of claim 146, wherein said dextrose solution comprises 5% to 70% dextrose in water.

148. (Withdrawn) The method of claim 147, wherein said dextrose solution comprises 5% or 10% dextrose solution.

149. (Withdrawn) The method of claim 98, wherein said secondary solvent comprises a parenteral infusion fluid.

150. (Previously Presented) The method of claim 97, wherein said solvent vehicle comprises glacial acetic acid and an aqueous lipid emulsion.

APPENDIX B

EVIDENCE

APPENDIX B

EVIDENCE

Exhibit 1: Stehle *et al.*, GB 145732, cited in Office Action dated September 24, 2004

Exhibit 2: Janoff *et al.*, U. S. Patent No. 6,406,713, cited in Office Action dated September 24, 2004

Exhibit 3: Szoka, U. S. Patent No. 5,277,914, cited in Office Action dated September 24, 2004